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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,982	04/25/2001	Scott L. Diamond	PENN0754	3650

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EXAMINER
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SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/763,982

Applicant(s)

DIAMOND, SCOTT L.

Examiner

Richard Schnizer, Ph. D

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 April 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4 and 6-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 8 is/are allowed.
- 6) ☒ Claim(s) 4,6,7 and 9-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's amendment submitted 4/16/04 has been entered.

Claims 1-3 and 5 were canceled as requested.

Claims 4 and 6-12 remain pending and are under consideration in this Office Action.

### ***Rejections Withdrawn***

The rejections under 35 USC 102 over Fan, over Sachdev, over Grondin, and over Birnsteil are withdrawn in view of Applicant's amendments.

The rejections of claims 8-12 under 35 USC 103 are withdrawn because there was no motivation in the prior art to select a NLS that interacts with transportin over other NLS s that do not interact with transportin.

### ***Compliance with Sequence Rules***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). This application clearly fails to comply with the requirements of 37 C.F.R.1.821-1.825. Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **The specification at page 17, line 24 discloses an amino acid sequence in excess of 3 amino acids that is not accompanied by a SEQ ID NO.** If this sequence

is listed in the current Sequence Listing, then the specification should be amended to include the appropriate SEQ ID NO in the passage referred to above. If this sequence is not in the current Sequence Listing, then Applicant must provide:

A substitute computer readable form (CRF) copy of the "Sequence Listing".

A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter***

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 7 was amended to require a cationic peptide scaffold of "less than 124 amino acids in length". Applicant points for support for this limitation to the specification at page 9 which teaches that a cationic scaffold can be 5-200 amino acids in length. However, this disclosure does not indicate that Applicant ever contemplated the precise embodiment of a peptide scaffold of "less than 124 amino acids in length". Because this limitation lacks written support in the specification, and there is no evidence that it was specifically contemplated, it represents new matter.

***Written Description***

Claims 4, 7, and 9-12 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4, and 7 are drawn to the genus of peptides comprising non-classical NLSs that do not interact with importin alpha or importin beta, but do interact with

transportin, wherein the peptides do not contain a classical NLS. Claims 9-12 are drawn to the genus of peptides comprising non-classical NLSs, wherein the peptides do not also contain a classical NLS.

For a discussion of the written description requirement as applied to genus claims, Applicant is referred to the interim guidelines on written description published December 21, 1999 in the Federal Register, Volume 64 Number 244, pp. 71427-71440 (also available at [www.uspto.gov](http://www.uspto.gov)). The following passage is particularly relevant.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The central issue in this analysis is whether the specification discloses a number of species which is representative of the claimed genus. The specification discloses two species of the claimed genus, i.e. M9 and HNS. The other species of non-classical NLS disclosed is KNS, which the specification teaches does not utilize the same import pathway as M9. As such, the Office concludes that KNS does not interact with transportin and is not a member of the claimed genus. The specification teaches that M9 and HNS show "some homology" (page 8, lines 17 and 18), but does not teach what homologous regions of M9 and HNS are required for transport and interaction with

transportin, and does not disclose the sequence of HNS. Further, the assertion of homology between M9 and HNS is not accepted by others of skill in the art. Fan et al (PNAS 95: 15293-15298, 1998) at page 15293, column 2, lines 4-6 of paragraph bridging pages 15293 and 15294 state that HuR (which comprises HNS) "does not however, have any M9-, KNS, or NES-like sequence, suggesting that it may contain a unique shuttling/NES motif." So, the specification discloses by complete structure only a single species of the claimed genus, and fails to disclose any correlation between structure and function that is shared by the members of the claimed genus. Further it is apparent from the teachings of Fan (1998) that the two disclosed species are substantially divergent in sequence, so it seems that there is substantial variation in the claimed genus. Furthermore, is not entirely clear that HNS is even a member of the claimed genus because Fan suggest that "HNS is a unique shuttling sequence with a transport mechanism potentially different from that of M9." See page 15297, column 1, second full paragraph. In view of this variability, and the failure to disclose relevant identifying characteristics such as a known or disclosed correlation between structure and the claimed function, the disclosure of only one or two species would not convey to one of skill in the art that Applicant was in possession of the claimed genus at the time of the invention.

### ***Response to Arguments***

Applicant's arguments filed 4/16/04 have been fully considered but they are not persuasive.

Applicant addresses the written description rejection at pages 7 and 8 of the response. Applicant argues that the Fan reference in fact teaches that M9 and HNS are homologous, and that one of skill in the art could readily recognize that structural and

functional relationship existed between M9 and HNS. This argument is unpersuasive for several reasons. First, Fan (1998) was published after the time of filing and is not indicative of the state of the art at the time the invention was filed. Second, Fan clearly demonstrates that even after the time of filing, those of skill in the art could not have discerned any structure/function relationship in common between M9 and HNS. Applicant argues to the contrary and points to Fig. 6B of Fan for support. However, in discussing Fig. 6B, Fan states that there is "no extensive homology between HNS and M9", and while noting that both sequences have a high serine and glycine content, states that the critical G274 residue of M9 is not conserved in HNS "suggesting that HNS is a unique shuttling sequence with a transport mechanism potentially different from that of M9." As such, Fan provides no support for the notion that it would be clear to one of skill in the art what conserved sequences provide the functions of transportin-dependent nuclear import. For these reasons the rejection is maintained

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 6 stand rejected under 35 U.S.C. 102(b) as being anticipated by Michael et al (Cell 82(3): 415-422, 1995).

Michael (1995) teaches a 38 amino acid peptide identical to SEQ ID NO: 3 that functions as a nuclear localization sequence of a fusion partner. See abstract and page



417, column 1, second paragraph to page 418, column 2, first paragraph. Thus Michael anticipates the claims.

Claim 4 stands rejected under 35 U.S.C. 102(b) as being anticipated by Michael et al (EMBO J. 16(12): 3587-3598, 1997).

Michael (1997) teaches the minimal nuclear shuttling domain (KNS) of hnRNP K protein, which was able to direct nuclear localization of a fusion partner. See paragraph bridging columns 1 and 2 on page 3589. Thus Michael anticipates the claims.

### ***Response to Arguments***

Applicant's arguments filed 4/16/04 have been fully considered but they are not persuasive.

With regard to the rejections over Michael (1995), Fan (1998), and Michael (1997), Applicant argues at pages 9 and 10 of the response that these references fail to teach the claimed functional limitations of transportin interaction, rather than importin alpha and beta interaction, to mediate nuclear pore targeting and import of molecules into the nucleus of cells. This argument is unpersuasive because each of the cited references teach the claimed structures, and show that nuclear transport occurs. The functional characteristics of the transport peptides are inherent in their structures, so the rejections are maintained.

### ***Conclusion***

Claim 8 is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

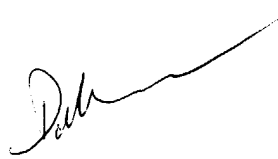
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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.



DAVE T. NGUYEN  
PRIMARY EXAMINER